MT-TK gene

mitochondrially encoded tRNA lysine

Normal Function

The *MT-TK* gene provides instructions for making a molecule called a transfer RNA (tRNA), which is a chemical cousin of DNA. Transfer RNAs help assemble protein building blocks (amino acids) into full-length, functioning proteins. The *MT-TK* gene provides instructions for a specific form of tRNA that is designated as $tRNA^{Lys}$. During protein assembly, this molecule attaches to a particular amino acid, lysine (Lys), and inserts it into the appropriate locations in the growing protein.

The $tRNA^{Lys}$ molecule is present in cellular compartments called mitochondria. These structures convert energy from food into a form that cells can use. Through a process called oxidative phosphorylation, mitochondria use oxygen, simple sugars, and fatty acids to create adenosine triphosphate (ATP), the cell's main energy source. The $tRNA^{Lys}$ molecule is involved in the assembly of proteins that carry out oxidative phosphorylation.

In certain cells in the pancreas, called beta cells, mitochondria also play a role in controlling the amount of sugar (glucose) in the bloodstream. In response to high glucose levels, mitochondria help trigger the release of a hormone called insulin. Insulin regulates blood sugar levels by controlling how much glucose is passed from the blood into cells to be converted into energy.

Health Conditions Related to Genetic Changes

Leigh syndrome

maternally inherited diabetes and deafness

A mutation in the MT-TK gene has been found in a small number of people with maternally inherited diabetes and deafness (MIDD), which is a condition characterized by diabetes and hearing loss, particularly of high tones. Less commonly, affected individuals have problems with their eyes, muscles, heart, or kidneys. The mutation involved in this condition changes a single DNA building block (nucleotide) in the *MT-TK* gene; the nucleotide adenine is replaced by the nucleotide guanine at gene position 8296 (written as A8296G). Researchers believe that the A8296G mutation impairs the ability of mitochondria to help trigger insulin release. In affected individuals, diabetes results when the beta cells do not produce enough

insulin to regulate blood sugar effectively. Researchers have not determined how the A8296G mutation leads to hearing loss or the other features of MIDD.

myoclonic epilepsy with ragged-red fibers

Several mutations in the *MT-TK* gene have been identified in people with myoclonic epilepsy with ragged-red fibers (MERRF). This condition is characterized by muscle twitches (myoclonus), recurrent seizures (epilepsy), abnormal muscle cells known as ragged-red fibers, and other problems with the nervous system. Most of the mutations involved in this condition change single nucleotides in the gene. One mutation causes about 80 percent of all MERRF cases. This genetic change replaces the nucleotide adenine with the nucleotide guanine at gene position 8344 (written as A8344G). The A8344G mutation impairs the ability of mitochondria to make proteins, use oxygen, and produce energy. Researchers have not determined how changes in the *MT-TK* gene lead to the specific signs and symptoms of MERRF. They continue to investigate the effects of mitochondrial gene mutations in various tissues, particularly in the brain.

A small number of people with a mutation in the *MT-TK* gene have some features of MERRF and some features of another mitochondrial disorder called mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS). These affected individuals are said to have MERRF/MELAS overlap syndrome. Additional signs and symptoms of this syndrome include recurrent severe headaches, muscle weakness (myopathy), difficulty coordinating movements (ataxia), hearing loss, and stroke-like episodes including a loss of consciousness. The mutation in the *MT-TK* gene that causes MERRF/MELAS overlap syndrome changes a single nucleotide in the gene. Specifically, it replaces the nucleotide thymine with the nucleotide cytosine at gene position 8356 (written as T8356C). It is unclear how this genetic change leads to the signs and symptoms of MERRF/MELAS overlap syndrome.

other disorders

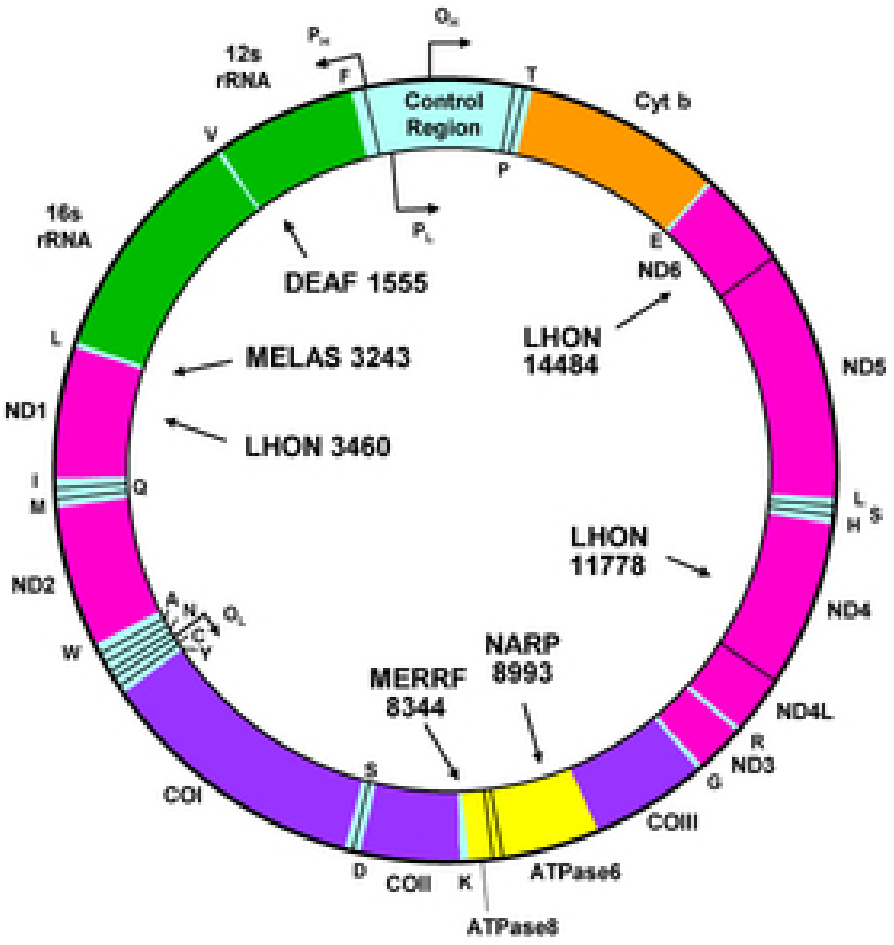
The A8344G mutation, which is the most common mutation found in people with MERRF (described above), can also cause a progressive brain disorder called Leigh syndrome. Signs and symptoms of this condition usually begin during infancy or early childhood and include vomiting, seizures, delayed development, myopathy, and problems with movement. Heart disease, kidney problems, and difficulty breathing can also occur in people with this disorder. Researchers have not determined why only some people with the A8344G mutation develop the signs and symptoms of Leigh syndrome.

A condition characterized by a weakened heart muscle (cardiomyopathy) and hearing loss is also caused by a mutation in the *MT-TK* gene. Affected individuals may also have myopathy and ataxia. This mutation replaces the nucleotide guanine with the nucleotide adenine at position 8363 (written as G8363A) within the gene. It is unclear

how this alteration in the *MT-TK* gene results in cardiomyopathy, hearing loss, and other symptoms.

Chromosomal Location

Molecular Location: base pairs 8,295 to 8,364 on mitochondrial DNA (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Other Names for This Gene

- mitochondrial tRNA-Lys
- MTTK
- trnK

Additional Information & Resources

Educational Resources

- Madame Curie Bioscience Database: Mitochondrial Translation System
  https://www.ncbi.nlm.nih.gov/books/NBK6292/#A27945
- Mayo Clinic Mitochondrial Disease Biobank
  http://www.mayo.edu/research/centers-programs/mitochondrial-disease-biobank/overview
- Neuromuscular Disease Center, Washington University: MELAS
  http://neuromuscular.wustl.edu/mitosyn.html#melas
- Neuromuscular Disease Center, Washington University: MERRF
  http://neuromuscular.wustl.edu/mitosyn.html#merrf
- The Cell: A Molecular Approach (second edition, 2000): The Genetic System of Mitochondria
  https://www.ncbi.nlm.nih.gov/books/NBK9896/#A1629

GeneReviews

- MELAS
  https://www.ncbi.nlm.nih.gov/books/NBK1233
- MERRF
  https://www.ncbi.nlm.nih.gov/books/NBK1520
- Mitochondrial Disorders Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1224
- Mitochondrial DNA-Associated Leigh Syndrome and NARP
  https://www.ncbi.nlm.nih.gov/books/NBK1173

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28MT-TK%5BTIAB%5D%29+OR+%28%28MTTK%5BTIAB%5D%29+OR+%28A8344G%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- TRANSFER RNA, MITOCHONDRIAL, LYSINE
  http://omim.org/entry/590060

Research Resources

- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=MT-TK%5Bgene%5D
- HGNC Gene Family: Mitochondrially encoded tRNAs
  http://www.genenames.org/cgi-bin/genefamilies/set/843
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=7489
- Mitomap: rRNA/tRNA mutations
  http://www.mitomap.org/MITOMAP/MutationsRNA
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/4566

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